Nutritional Problems in Cats: Taurine Deficiency and Vitamin A Excess

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SUMMARY

Two nutritional problems of the cat are reviewed. One represents a deficiency of taurine, the other vitamin A toxicity. Taurine deficiency in cats is insidious because the progressive retinal degeneration induced may go unnoticed until the damage is advanced and irreversible. Both rods and cones undergo degeneration along with the underlying tapetum lucidum. The hyperreflective focal lesion is easily observed in the area centralis with an ophthalmoscope and has been previously identified as feline central retinal degeneration. This lesion is not reversed by taurine supplementation, even though the remaining retina may be saved from further degeneration. The cat requires dietary taurine, found in meat and fish, because it cannot synthesize enough to meet demands for bile acid conjugation and tissue metabolism, especially those of muscle and central nervous system.

Vitamin A toxicity is not commonly observed in cats but may occur if cats are fed beef liver in which appreciable vitamin A is stored. Cats exhibit muscle soreness and hyperesthesia, especially along the neck and forelimbs where bony exostoses of cervical verterbrae and longbones are common. The diagnosis is readily made from radiographs. The response to removal of vitamin A from the diet is generally rapid and, unless the toxicity has been chronic in young kittens, recovery is generally satisfactory.

RÉSUMÉ

Problèmes nutritionnels, chez le chat: déficience en taurine et hypervitaminose A

Cet article présente deux problèmes nutritionnels du chat, dont l'un correspond à une déficience en taurine et l'autre, à une hypervitaminose A. La déficience en taurine, chez le chat, évolue de façon insidieuse, parce que la dégénérescence rétinienne qu'elle provoque peut passer inaperçue, jusqu'à ce qu'elle ait atteint un stade avancé et irréversible. Les bâtonnets et les cônes subissent une dégénérescence, en même temps que le *tapetum lucidum* sous-jacent. La lésion focale de réflexibilité excessive se détecte facilement, dans la région centrale, avec un ophtalmoscope, et on l'a déjà identifiée comme la dégénérescence rétinienne centrale féline. L'addition de taurine aux aliments ne guérit pas cette lésion, mais elle protège le reste de la rétine d'une dégénérescence plus marquée. La viande rouge et le poisson contiennent la taurine que requiert le chat, parce qu'il ne peut en synthétiser suffisamment pour satisfaire à la demande de conjugaison à l'acide cholique biliaire et à celle du métabolisme tissulaire, spécialement celui des muscles et du système nerveux central.

L'hypervitaminose A ne s'observe pas souvent, chez les chats; elle peut cependant se produire lorsqu'on les nourrit avec du foie de boeuf, lequel contient une quantité appréciable de vitamine A. Les chats atteints manifestent de la myalgie et de l'hyperesthésie, surtout le long du cou et des membres antérieurs où les vertèbres cervicales et les os longs présentent beaucoup d'exostoses. Les radiographies permettent de poser un diagnostic, sans difficulté. Le retrait de la vitamine A de la diète donne généralement un résultat rapide et la guérison s'effectue de façon satisfaisante, à moins que l'hypervitaminose A n'ait atteint un stade chronique, chez les chatons.

INTRODUCTION

With the surge in affluence since the second World War, pets in developed countries have become increasingly subjected to a captive feeding regimen of a largely urban populace. By and large the pet food industry has responded to the need and introduced packages of "total nutrition" in highly palatable forms. As a result, many pets have entered an era of increased food consumption and decreased physical activity. Like their affluent owners before them, this trend has been associated with a growing incidence of obesity and diabetes mellitus, particularly in dogs. Whereas these problems will require our attention in the immediate future, there are two specific nutritional problems of cats that are of continuing concern and which have been investigated in some detail. At different ends of the nutritional spectrum, one syndrome is to be discussed represents deficiency (taurine deficiency) and the other, toxicity (vitamin A excess).

TAURINE DEFICIENCY

For several years (since 1963) a blindness in cats has been recognized clinically that is characterized by central retinal degeneration (5,22). Originally thought to occur as a result of an inherited defect (22), it is now generally agreed that this particular retinopathy results from a deficiency of dietary taurine (2,4,10,18).

Taurine is a sulfonic amino acid, i.e. a sulfonic acid moiety is found in the usual carboxylic acid location of glycine. Because of this structural difference, taurine cannot be incorporated into peptides or proteins and thus remains free within cells and tissues, except for its binding to bile acids. Essentially restricted to the animal kingdom, taurine is synthesized in mammals by the conversion of the essential amino acid, methionine, to cysteine and finally to taurine during normal sulfur amino acid metabolism.

The question arose as to why cats should be affected by a lack of dietary taurine when no other mammals apparently suffer from the deficiency. A clue to the experimental approach

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to this problem came from the observation that kittens fed certain semipurified diets routinely developed the characteristic retinal lesion and blindness (11,25) which was associated with depletion of plasma taurine (10) and abnormal retinal function (20,23). Subsequent investigation revealed that despite added methionine or cysteine in the diet, taurine depletion still occurred (6). This reduced the possibility that poor synthesis resulted from inadequate levels of the dietary precursors, methionine or cysteine needed for taurine formation, and demonstrated that only dietary supplementation of the meager taurine synthetic capacity of cats would prevent the retinal degeneration. Since it was still not clear whether the cat might synthesize taurine by fixation of sulfate to serine and that dietary sulfate was limiting or whether an obvious cofactor such as vitamin B_6 was limiting, experiments were undertaken to test these possibilities. The results obtained were negative (16,24), indicating that taurine itself was an essential dietary component for the cat required for prevention of the retinal degeneration.

Additional research has revealed that the lesion observed ophthalmoscopically may not strictly represent photoreceptor cell damage, but may be associated with a concommitant degeneration of the underlying tapetum lucidum as well (28). This highly organized, specialized cellular layer of the choroid is designed to reflect light throughout the retina to enhance visual sensitivity, especially at night.

Retinal and tapetal degeneration and taurine function — The idea that a single amino acid should be essential for a specific physiological function such as vision was unique and intriguing. Or, stated another way, it seemed peculiar that taurine should only be required by the retina and tapetum of the cat. Research designed to explore this possibility is still in progress, but studies by others concerning taurine function provide certain clues. In the first place considerable taurine appears in the inner and outer segments of photoreceptor cells where it is thought to influence calcium and potassium ion flux across the photoreceptor pigment epithelial cell barrier (13). It is hypothesized that without taurine

the photoreceptor "collapses" and becomes disrupted and dysfunctional. This leads to photoreceptor cell death with eventual atrophy and loss of cells resulting in irreversible blindness. Interestingly, if taurine is fed during the period of outer segment disorganization before the photoreceptor cell is lost, the rod outer segment reorganizes and regains its functional capacity, much like the situation in vitamin A deficiency. By contrast, cone function may never be restored totally (11,23). In the tapetal cell of the cat, taurine appears to be linked with zinc in the membrane surrounding and stabilizing the specialized intracellular tapetal rod. Taurine loss results in breakdown and disintegration of the rod structure (27,28).

When it was found that plasma and retina were losing taurine, other tissues were examined to determine whether this was a generalized phenomenon or restricted to those two taurine pools (16,21). Surprisingly most tissues experienced a dramatic decrease in taurine concentration, as much as tenfold or more. Three tissues were noteworthy for their conservation of taurine: bile, retina and olfactory bulb, in that order. The data suggest that these three tissues, especially bile, are especially good at taurine conservation and that taurine probably plays an important role in each. Its role in retinal function has already been discussed, but the possible function of taurine in olfaction is less obvious. As for bile, it is known that taurine conjugated bile acids are more effective for solubilization and absorption of fat than their glycine counterparts.

Although the olfactory bulb shrinks in size during taurine depletion, it is not known whether the altered size is associated with an impaired sense of smell or taste. During taurine depletion taurine conjugation of the bile acid pool in cats is not reduced appreciably. When it does occur, the cat's liver secretes unconjugated bile acids rather than switching to conjugation with glycine, a switch that occurs with most other species (15). Thus, the combined misfortune of poor taurine synthesis plus the inability to substitute glycine for taurine during bile acid conjugation appear to be responsible for the cat's dependency on a dietary

source of taurine. Interestingly, the dog cannot conjugate bile acids with glycine either, but unlike the cat, dogs synthesize a considerable amount of taurine (15,19).

Other effects of deficiency —Although inadequately documented at this date, it appears that taurine is also required for maximal growth in the newborn kitten (unpublished data), with the effect being even greater than that described in monkeys (12). Continued investigation of these various aspects of taurine metabolism will ultimately provide a better appreciation of its function and dietary requirement by the cat.

Taurine requirements of various species — Taurine deficiency does not appear in species other than the cat for several reasons that depend on the principles of supply and demand (14). A certain amount of taurine is probably supplied by endogenous synthesis in all species, whereas a significant exogenous dietary contribution is available to omnivorous and carnivorous species since taurine is usually abundant in meat and fish. Demand, on the other hand, would be created primarily by bile acid conjugation and an expanding muscle mass during growth. Thus, some species with an extraordinary synthetic ability (rat and dog) can meet the body's demand even though their bile acids are predominantly conjugated with taurine. Others have a lesser synthetic capability, but reduce demand by conjugating their bile acids with glycine (rabbit, guinea pig). Still others (man, Old World monkeys) have poor synthetic ability and prefer to conjugate with taurine, but switch to glycine when dietary taurine is low. Ordinarily tissues conserve their pool of taurine when threatened by depletion, including most tissues of the cat (16). The demise of the cat is thought to result from poor synthesis coupled with a large demand for bile acid conjugation, it being unable to convert to glycine conjugation (21). The kitten has the added disadvantage of rapid growth and expansion of its muscle mass, which represents the major mass of body taurine. An unanswered question in the cat is the demand placed on the cysteine pool for the synthesis of

felinine, a sulfur amino acid excreted in large amounts in cat urine (3). Since cysteine is also the precursor for taurine, its incorporation into felinine may result in reduced synthesis of taurine.

This combination of factors makes dietary taurine an essential nutrient for cats. The minimum amount required in cat diets is not exactly known since the age, rate of growth, level of dietary protein and amount of sulfur amino acids present are all thought to have an impact. However, it is unlikely that deficiency signs would develop below 500 ppm in the diet, and 750 ppm is probably sufficient for exceeding tissue storage capacity (18). In the past, certain pet foods, based largely on cereals, were found to have low concentrations of taurine that resulted in taurine depletion when consumed by cats (1).

VITAMIN A TOXICITY

Toxicity due to this fat-soluble vitamin is unusual in the animal kingdom because the main source of dietary vitamin A for most species is in the form of its precursor, the plant pigment β-carotene. Whereas carotene is not toxic and its hydrolysis and absorption as retinol are carefully regulated by the gut, preformed vitamin A can be extremely toxic if consumed in large amounts. Only carnivores consume all, or most, of their vitamin A as preformed retinyl palmitate stored in the tissues, particularly the liver, of their prey. This peculiarity again renders the cat vulnerable to dietary perturbation of a nutritional nature.

Clinical syndrome — Because cats are carnivorous and are occasionally fed an almost total liver diet, they are potentially subject to overconsumption of vitamin A. This is not common, but sporadic cases still occur when cats have access to a constant supply of liver containing a relatively high concentration of vitamin A. Most recently such circumstances have been reported from Australia where cats received a ready supply of liver from cattle in local slaughter houses (26). Affected cats typically develop stiffness and soreness of muscle, hyperkinesis, and extreme tenderness of joints, including the cervical skeleton. The latter is associated with bony exostoses that develop along the muscular insertions of the cervical vertebrae, ribs, and long bones of the fore limbs. The condition is usually accompanied by anorexia, weight loss, exophthalmia, and an unkept appearance and may lead to moist eczema, alopecia, cracking scaly dermatitis, ascites and death. Livers from affected cats may concentrate vitamin A at extraordinary levels (25 000 μg/g compared to the normal 100-250 μg/g). The condition has also been reported in England and is known to occur in the United States and New Zealand, but was originally described in Uruguay (17).

Deforming cervical spondylosis, as the condition has been called (26), can be a crippling clinical entity in cats from two to nine years of age. These investigators reproduced the syndrome in weanling kittens by feeding vitamin A at a level of 20 000-30 000 μg/kg body weight/day, or 100 times the normal intake for a period of six months. At lower doses cervical spondylosis, alone, without other side effects, may be the only clinical sign. Removing vitamin A from the diet tends to ameliorate the toxic signs, including the peculiar sensitivity of the cervical skeleton to palpation. Bone changes persist although substantial remodeling toward normal occurs with time.

High doses (8) of vitamin A consumed for a short period of time by suckling kittens resulted in acute toxicity with residual depression of bone growth during subsequent development. As in other species this defect was thought to represent a cytotoxic influence of vitamin A on osteoblasts and chrondrocytes.

Toxocity is associated with temporary infertility in males, but surprisingly not in females where relatively normal kittens may be conceived and delivered.

Mechanisms of vitamin A toxicity — Most circumstances associated with this toxicity in cats are characteristic of excess vitamin A. It is noteworthy that the level of vitamin A required to induce toxicity in rats, cats and dogs ($>$ 20 000 μg/kg) is approximately ten times greater than the threshold for most species, including man. A logical explanation for this difference might be linked to retinol binding protein (RBP) synthesis and metabolism. A ready supply of RBP is normally bound to vitamin A during its transport in blood, thereby protecting cell membranes and tissues from the cytotoxic effect of a large amount of unbound or free retinol (9). Thus, the cat would appear to have a high capability for binding vitamin A and protecting its tissues.

The lesions observed in cats probably reflect both the initial physiopharmacological influence of vitamin A stimulation (controlled delivery of large amounts of vitamin A) followed by its cytotoxic effect (osteoblast and chrondrocyte death) which occur with continuous consumption of large quantities of vitamin A and exposure to unbound retinol. Most species appear to pass through the physiological threshold quickly and experience the cytotoxic aspect, and thus fail to develop the full spectrum of bone lesions observed in the cat. Removing vitamin A from the diet generally results in rapid recovery in the cat. It should be pointed out that additional studies are needed to demonstrate whether the toxicity ascribed to vitamin A may not be influenced by other dietary imbalance(s), although the unfavorable calcium phosphorus ratio present in a high meat diet has been ruled out (7).

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ABSTRACT

Fregin, G.F. General discussion of physiologic observations recorded on 117 horses during 100-mile endurance rides. Proceedings of the Annual Convention of the American Association of Equine Practitioners (1980) 25: 315-321. (Sch. Vet. Med., Univ., New Bolton Center, Kennett Square, Pennsylvania 19348, USA).

Observations were made on the day before the ride, at stops every three hours, and at the end. Packed cell volume increased by 20% after 30 miles and remained high. Total plasma protein was increased by 7% at the first stop, returned to pre-ride levels by 83 miles and was only increased by 2% at the end. Blood glucose decreased by 22.5% and free fatty acids increased fivefold. There was little change in blood lactates. Creatinine phosphokinase increased fourfold. Mean Cl and Ca levels were reduced by 8-10%, and P and K by 45 and 14%, respectively. The importance of expert supervision of such rides is emphasized.

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